ANEMIAS OF PREGNANCY

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A DECREASE in the hemoglobin concentration, hematocrit, and erythrocyte count of the peripheral blood occurs during pregnancy. True anemia of pregnancy has been defined as a condition in which these constituents are reduced below the level considered physiologic for the period of gestation.[1] Various minimal hematologic standards for normal pregnancy have been proposed.[1, 2, 3] For this study a hemoglobin of 10 Gm. per cent, a hematocrit of 33 per cent, and an erythrocyte count of 3.36 million per cubic millimeter were considered as the minimal normal values between the twelfth and the thirty-sixth week of pregnancy.[2]

Many observers have described satisfactory therapeutic results using iron preparations alone or in combination with other substances.[1, 4, 5, 6, 7] Others have ascribed little efficacy to these agents.[2, 8] In view of these discrepancies we feel that adequate comparison with simultaneously observed controls is lacking. As a result, this study was undertaken to review the cases of anemia of pregnancy followed at the Chicago Lying-in Hospital during the past several years.

Initial and periodic hemoglobin determinations are very important parts of prenatal and postpartum care. The usual methods for determining hemoglobin—either with the visual or photoelectric colorimeter—require very small amounts of blood, 0.02 ml. and dilutions of 100 to 400 times. Thus the combined error of the pipette and chamber, as well as the technician may be 7 to 15 per cent. The hematocrit and erythrocyte count are methods for determining the number of red blood cells per unit of blood. The hematocrit has a closer correlation with the hemoglobin concentration than the red cell count, because the error in the former is approximately 2 per cent, while the minimum error in the red cell count is over 8 per cent. For over ten years we have been using the hematocrit determination on heparinized blood as a screening method. Any patient who is less than twelve weeks pregnant or more than six weeks post partum whose hematocrit is less than 37 volumes per cent is referred to the antepartum anemia clinic. Between twelve weeks and thirty-six weeks gestation the lower limit of the hematocrit is 30, and between thirty-six weeks and term the lower limit is 32 volumes per cent. The procedure in the anemia clinic is to obtain additional history and special examinations as to possible causes for the anemia. A diet history is obtained in some instances. The hemoglobin,

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hematocrit, red cell count, leucocyte count, and differential determinations are made. The various indices, mean corpuscular hemoglobin, and cell volume, etc., are determined and the anemia classified. For purposes of this study, all cases complicated by blood loss, toxemia, and infection were excluded.

After a preliminary observation period of two to six weeks during which the determinations were repeated, therapy was begun. All treated cases received iron in doses accepted to be adequate.* Also, in certain of the cases accessory hematopoietic substances such as vitamins of the B complex, desiccated hog's stomach, and liver extract were administered in addition to the iron. In the graphs and tables these are included under the heading: Iron and Vitamins. After the institution of therapy the cases were followed at biweekly intervals until three to six months post partum with periodic blood studies. Patients with hemoglobin concentrations of six grams per cent or less were hospitalized for a more detailed study. In some cases transfusions of whole blood served as the principal therapy given or as a supplement to other treatment.

Results

Two hundred fifty cases were studied. These have been classified as to mean corpuscular volume[9] and therapy administered (Table I). The mean corpuscular hemoglobin concentration[9] was determined in each case, and it was found that 42 per cent were normochromic, 56 per cent hypochromic, and 2 per cent hyperchromic. At the time of their first visit 57 per cent of the entire group were anemic. This represented 61 per cent of the treated group and 48 per cent of the controls.

TABLE I

		GAIN OF Hb IN GM. IN 21 DAYS				
		A	B	C	D	E
	NO. OF CASES	DECREASED OR UNCHANGED	0 TO 1.5 GM.	1.6 TO 3.3 GM.	OVER 3.3 GM.	MEAN GAIN GM.
Macrocytic						
Controls	12	5	5	1	1	0.82 ± .20*
Iron alone	31	10	15	6	0	0.73 ± .09
Iron and vitamins	19	6	8	4	1	0.92 ± .15
Transfused	2					
Subtotal	64					
Microcytic						
Controls	39	8	23	5	3	0.86 ± .09
Iron alone	53	11	24	17	1	1.24 ± .09
Iron and vitamins	32	9	13	8	2	1.04 ± .14
Transfused	9					
Subtotal	133					
Normocytic						
Controls	25	13	11	1	0	0.24 ± 0.6
Iron alone	27	10	12	5	0	0.73 ± .12
Transfused	1					
Subtotal	53					
Total	250					

*Probable error of mean.

*Iron was prescribed in the following daily doses: Ferrous sulfate, 1.0 Gm.; Ferric ammonium citrate, 5.0 Gm.; or Ferrous Carbonate, 5.0 Gm.

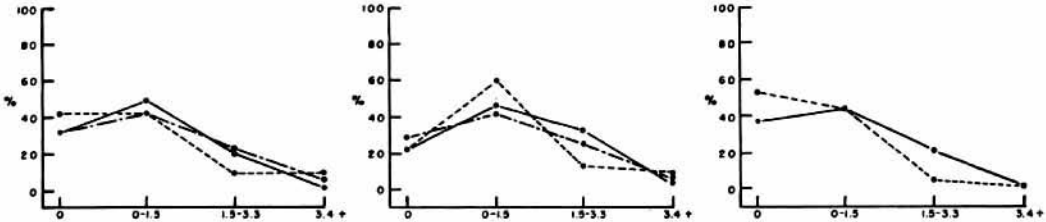

Fig. 1.

TABLE II

COMPARISON OF TREATED GROUP WITH CONTROLS AT BEGINNING OF OBSERVATION PERIOD				
	MEAN AGE	MEAN NO. OF PREG.	MEAN Hb	MEAN WEEK OF PREGNANCY
Untreated controls	28.3 ± .5	3.2 ± .2	9.1 ± .09	31.4 ± .4
Treated group	27.5 ± .3	3.2 ± .1	9.0 ± .06	31.2 ± .3

TABLE III

	MACROCYTIC		MICROCYTIC		NORMOCYTIC	
	Hb	SD*	Hb	SD*	Hb	SD*
Controls	10.2	0.7	9.6	1.4	9.8	1.3
Treated group	11.1	1.4	10.6	1.9	11.3	1.7

*SD. Standard deviation.

During adequate therapy the expected rate of hemoglobin formation is 0.078 Gm. per day, and the maximum is reached between the second and fourth week.[10, 11] For this reason a twenty-one-day observation period was selected in order to evaluate the effects of treatment. At the beginning of this period the treated group showed no significant differences from the controls (Table II).

The gain in hemoglobin concentration in the various groups during the three weeks of observation is recorded in Table I (Columns A to D). Inspection of these data reveals that the number of cases showing the expected gain in hemoglobin during this observation period, 1.6 Gm. in twenty-one days, is only slightly greater in the treated groups than in the controls. Fig. 1 presents these data in graphic form, the gain in grams of hemoglobin being plotted along the abscissa, and the percentage of cases along the ordinate. When the mean values in the separate groups are compared, the difference between the controls and the treated cases is not statistically significant (Table 1, Column E).

Comparison of the hemoglobin values of the treated groups and the controls at term failed to reveal any significant differences between the two (Table III). Further, while 51 per cent of the controls were anemic at term, 27 per cent of the treated group were still anemic at that time.

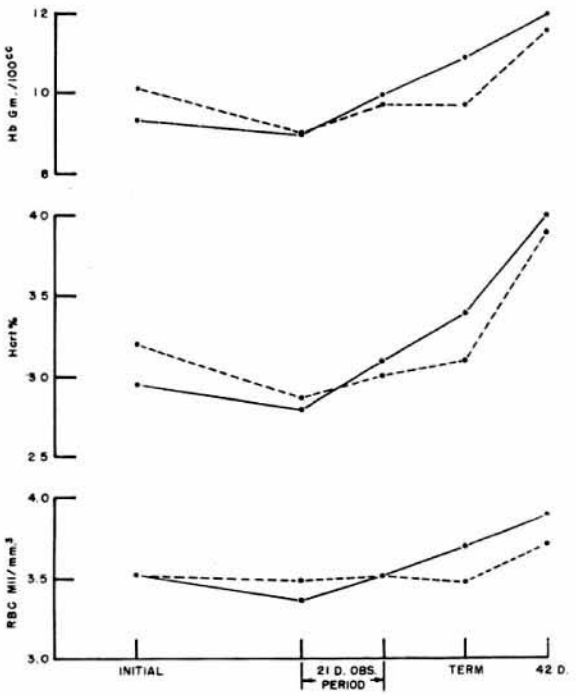

Fig. 2.

Many patients did not return for postpartum examinations, and therefore data were not uniformly available for comparison. The hematologic values of both groups, however, showed a rapid return to normal levels during this period (Fig. 2).

Diet histories of forty-two patients were analyzed by our nutritionist. Using the National Research committee's criteria for iron, and Burke's criteria for protein, she classified the diets as follows: poor iron and poor protein intake—14 per cent; poor iron, fair protein—31 per cent; poor iron and good protein—17 per cent. Thus 62 per cent had a low intake of iron. However, these diets may not be as deficient as they seem to be because they were based on patients' estimates, and we have learned that they are inaccurate and that the food must be weighed and recorded immediately. We are now doing this.

In certain cases transfusions of whole blood served as the principal therapeutic agent as indicated above. In these, transfusions were given as emergency measures because of rapidly falling hemoglobin values. Also, in five of the controls and in eleven of the treated cases, transfusions were administered after the completion of the twenty-one-day observation period when the patient had reached term before the hemoglobin had returned to normal levels. No hematologic data on the transfused cases are included here, as blood was uniformly given in quantities adequate to bring the hemoglobin to normal levels.

Discussion

The plasma volume during pregnancy increases 25 per cent and the red cell volume only 23 per cent, thus accounting for the physiologic anemia of pregnancy.[12] Reported bone marrow studies have revealed a normal erythroid pattern, and served to confirm the concept that this condition arises from hydration alone.

The cases in the present study represent those in which the hematologic findings fell below the minimal physiologic values. Changes in the peripheral blood may reflect both pathologic and physiologic processes simultaneously and their detection is characterized by certain inherent errors.[2] As a result of these factors the effects of any therapeutic agent must be evaluated cautiously.

Classically, microcytic hypochromic anemias are associated with iron deficiency. During pregnancy an inadequate diet, defective absorption from the gastrointestinal tract, and increasing fetal demands have been accused of precipitating this condition. Wolff and Limarzi[13, 14] report a normoblastic hyperplasia of the bone marrow in such cases. These workers and others[1, 5, 6] conclude that these anemias are the result of an iron deficiency and can be corrected by administering simple iron salts. Some workers stress the importance of diet in their prevention and correction.[1, 15, 17] Others indicate that although an adequate diet is important from the standpoint of maternal health, the quality of the diet has little effect on the hematologic findings except in the extremes.[3, 8, 16] Changes in the gastrointestinal secretory function occur in most pregnant women,[17] yet no significant correlation exists between the decreased gastric acidity and the incidence of anemia.[3] Further, studies with radioactive materials during pregnancy have revealed that iron is absorbed at two to ten times the normal rate.[18] The amount of iron necessary for fetal growth is negligible during the first twenty-eight weeks and yet it is during this period that there is the greatest fall in the maternal hemoglobin concentration. It is only during the last twelve weeks, when the fetal weight increases from approximately 1,000 Gm. at twenty-eight weeks to 3,400 Gm. at term, that the iron requirement of the fetus becomes appreciable. But even at term, when the actual amount of iron required by the fetus is greater, the total fetal content is only 280 mg., which could be furnished by the iron from 600 c.c. of maternal

blood. Furthermore, it is during this last twelve weeks that the maternal hemoglobin concentration is either stationary or is increased. Thus, during the maximum fetal requirement, the hemoglobin concentration also increases.[2, 8]

The results of the present study indicate that during pregnancy the rate of hemoglobin formation is not significantly altered by the administration of iron alone or in combination with accessory substances. In the light of the foregoing material this suggests that these anemias are not due to a simple iron deficiency, but that some other factor is lacking or that the defect lies in the mechanism of postabsorptive iron utilization.

The "pernicious-like" or megaloblastic anemia of pregnancy occurs only rarely.[19] Several workers suggest that the diagnosis can only be made from studies of the bone marrow and that the peripheral blood findings are often misleading.[13, 14, 20] It is unlikely that the macrocytic anemias in the present series are examples of the megaloblastic type of anemia.

Summary

Two hundred fifty cases of anemia in pregnancy were studied to evaluate the effects of treatment with iron alone and in combination with accessory factors. Controlled observations indicate that the administration of these substances does not increase the rate of hemoglobin formation significantly.

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